

Lipid profiles and fibrinogen levels in coronary heart disease and dyslipidemic patients in Dr. Sardjito Hospital Yogyakarta

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ABSTRACT

Epidemiological studies indicated that fibrinogen and dyslipidemia were important risk factors for cardiovascular disease (CVD). For several populations in the world, increase in cholesterol level and decrease in high-density lipoprotein cholesterol (HDL-C) were risk factors for coronary heart disease (CHD). The role of elevated fibrinogen in thrombosis suggests that it may be the causal pathway for certain risk factors of CHD. The aim of this study is to determine the role of lipid profile and fibrinogen level as risk factors of coronary heart disease. Blood samples were obtained from CHD patients, dyslipidemic patients, and controls after they had fasted. Lipid profiles and fibrinogen level of CHD and dyslipidemic patients were determined and compared with controls. There were 92 subjects in this study, consisted of 35 CHD patients, 31 dyslipidemic patients, and 26 controls. There were significant difference in triglyceride level between CHD and dyslipidemic patients, also between dyslipidemic patients and controls ($p < 0.05$). Significant difference in level of cholesterol also existed between CHD patients and dyslipidemic patients, also between CHD patients and controls ($p < 0.05$). In dyslipidemic patients, decreased in HDL-C level was risk factor for CHD. Meanwhile for controls, high level of cholesterol and LDL-C also low level of HDL-C were risk factor for CHD, but fibrinogen level was not risk factor for CHD. In conclusion, lipid profile was risk factor for CHD whereas fibrinogen level was not risk factor for CHD.

Keywords: lipid profile – fibrinogen - coronary heart disease - dyslipidemia

INTRODUCTION

Fibrinogen is one of the main parts of blood plasma protein, and it strongly affects the development of clot, rheological reaction, and platelet aggregation. Fibrinogen also has impact on blood vessel wall and is a strong acute phase reactant. Increase in fibrinogen level was associated with the increase risk of CHD stroke, myocardial infarction (MI), and peripheral arterial diseases.¹⁻⁶ With immuno-precipitation, fibrinogen showed strong association with cardiovascular diseases, therefore fibrinogen level might be used as screening tool to identify the risk of thrombosis.⁷ Almost half of coronary artery disease patients had higher fibrinogen level compared with normal people.^{2,3,8-10} Occlusive thrombi were found in most cases of

acute myocardial infarction, sudden death caused by heart ischemia, and unstable angina. Thrombosis is the main mechanism of atherosclerosis complication.¹¹⁻¹³ Atherosclerotic lesions, that will form plaques, consist of extracellular hydrophobic lipid accumulation, lipid-containing macrophages, smooth muscle cells, and proteins in the endothelial surface of artery. It was assumed that increasing fibrinogen related with initial plaque formation, caused by acute phase response.¹⁴⁻¹⁶ The association of high fibrinogen level with pathogenesis of atherosclerosis is supported by the fact that fibrinogen induces disorganization and migration of endothelial cells, stimulates smooth muscle cell proliferation, and increases the release of growth factors from endothelial cells.²

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Dyslipidemia, especially high cholesterol level, is an indicator of liver function and increase risk of CVD,¹⁷⁻¹⁹ whereas the role of triglyceride level as risk factor of CHD is still controversial.²⁰ The aim of this study was to determine the role of fibrinogen and lipid profile as risk factor of CHD.

MATERIALS AND METHODS

Subjects

This was a cross-sectional study. Subjects of this study were CHD and dyslipidemic patients who visited Dr. Sardjito Hospital Yogyakarta and were obtained by consecutive random sampling. The diagnosis of CHD was established by internist. Dyslipidemic patients were patients with one abnormality in the lipid level, while the elderly aerobic group at Banteng village, Sleman district, Yogyakarta were enrolled as control groups. The protocol of this study was approved by the Health Research Ethics Committee of Faculty of Medicine, Gadjah Mada University, Yogyakarta.

Chemical analysis

Blood samples were obtained from the subjects and controls after they had fasted. Plasma was

separated from the blood to determine lipid profiles and fibrinogen level. To determine total cholesterol, HDL-C, and triglyceride levels, plasma samples were analyzed using Diaysis kit in Biochemistry Laboratory, Department of Biochemistry, Faculty of Medicine, Gadjah Mada University, Yogyakarta. Low-density cholesterol level was determined using Friedewald equation (1972). Fibrinogen level was measured employing Fibrinoquik kit in Clinical Pathology Laboratory, Dr. Sardjito Hospital, Yogyakarta.

Data analysis

Group differences of continuous variables such as lipid profiles and fibrinogen levels were compared using Anova and t-test. Odd Ratio was calculated using logistic regression analysis.

RESULTS

A total of 92 subjects which consisted of 35 CHD patients, 31 dyslipidemic patients and 26 controls were enrolled in this study. Data of age, BMI (Body Mass Index), blood pressure, lipid profile and fibrinogen levels of the subjects are shown in TABLE 1 and FIGURE 1.

TABLE 1. Lipid profile and fibrinogen level of CHD patients, dyslipidemic patients, and controls (mean \pm SD)

	CHD patients (n=35)	Dyslipidemic patients (n=31)	Control (n=26)	P
Male	23	12	15	>0.05
Female	12	19	11	>0.05
Age (years)	61.24 \pm 9.31	56.84 \pm 8.30	57.19 \pm 8.50	>0.05
BMI (kg/m ²)	23.8 \pm 3.0	25.2 \pm 3.7	24.0 \pm 3.35	>0.05
Systolic BP (mmHg)	140.61 \pm 17.13	138.06 \pm 19.95	137.31 \pm 19.56	>0.05
Diastolic BP (mmHg)	83.94 \pm 10.29	87.10 \pm 9.57	89.04 \pm 12.96	>0.05
Cholesterol (mg/dL)	199.740 \pm 32.272 ^a	154.490 \pm 66.470 ^a	154.710 \pm 37.580 ^a	<0.05
HDL-C (mg/dL)	45.142 \pm 14.684	48.816 \pm 10.014	50.833 \pm 7.429	>0.05
LDL-C (mg/dL)	126.98 \pm 38.272	143.39 \pm 35.025	97.430 \pm 25.010	>0.05
Triglyceride (mg/dL)	132.900 \pm 71.069 ^b	239.010 \pm 48.816 ^b	117.560 \pm 51.476 ^b	<0.05
Fibrinogen (mg/dL)	291.20 \pm 90.38	315.38 \pm 79.31	349.330 \pm 70.33	>0.05

^a Significant difference between CHD patients & dyslipidemic patients and also CHD patients and controls (p<0.05)

^b Significant difference between CHD patients and dyslipidemic patients and also dyslipidemic patients & controls (p<0.05)

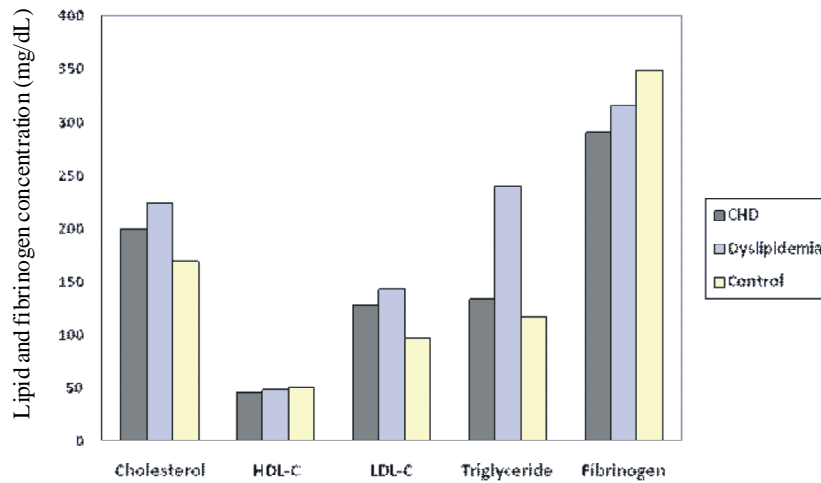


FIGURE 1. Lipid and fibrinogen concentration in CHD, dyslipidemic patients and controls

Statistical analysis using Anova showed significant differences ($p < 0.05$) in total cholesterol and triglyceride level between CHD patients, dyslipidemic patients, and controls (TABLE 1). Meanwhile t-test results showed there were significant difference in triglyceride level between CHD patients and controls also between dyslipidemic patients and controls ($p < 0.05$). Furthermore, there were significant difference in cholesterol level between CHD patients and dyslipidemic patients,

and also between CHD patients and controls ($p < 0.05$).

Odds ratio of lipid profile and fibrinogen levels between CHD patients and controls were shown in TABLE 2. This study observed that high level of cholesterol and LDL-C also low HDL-C level were high risk factor for CHD, but blood pressure, triglyceride and fibrinogen level were not risk factors (TABLE 2).

TABLE 2. Odd Ratio of lipid profile and fibrinogen levels between CHD patients and controls

	CHD N = 35	Controls N = 26	OR (CI 95%)
Systolic = 140 mmHg	20 (57%)	14 (54%)	1.14 (0.36-3.60)
Diastolic = 90 mg/dL	13 (37%)	16 (61%)	0.37 (0.11-1.19)
Cholesterol > 200 mg/dL	15 (43%)	1 (4%)	14.77 (1.74 -327.02)
Triglyceride > 150 mg/dL	8 (23%)	7 (27%)	0.80 (0.21 -3.02)
HDL-C < 35 mg/dL	6 (17%)	1 (4%)	5.17 (0.54-121.93)
LDL-C > 130 mg/dL	16 (46%)	4 (15%)	4.63 (1.16 -19.94)
Fibrinogen >350 mg/dL	8 (23%)	11 (54%)	0.40 (0.11 -1.40)

DISCUSSION

A study by Benderly¹⁰ showed that high blood pressure, both of systolic and diastolic blood pressure, were risk factor for CHD. However, this study observed that blood pressure was not significantly different between CHD patients and controls. This indicated that blood pressure was not risk factor for CHD. It was probably because that CHD patients with high blood pressure usually consume drugs to maintain their blood pressure. Lipid profiles in this study were significantly different between CHD patients, hyperlipidemic patients, and control groups, in which cholesterol, triglyceride level and dyslipidemia being the high risk factor for CHD. Sgarbosa²¹ suggested that high cholesterol level would accumulate in arterial wall and formed atheroma plaque that would stimulate CHD. Therefore, the higher HDL-C level the lower risk of CHD. It was in contrast with LDL-C and triglyceride levels, in which increase in LDL-C and triglyceride levels tend to cause CHD.²² It was understandable that in this study CHD patients had showed lower HDL-C level than dyslipidemic patients and controls, and higher cholesterol level than controls. The pathophysiology of atherosclerosis is a complex interaction between cellular compounds in atherosclerotic lesion.

Fibrin structure did not only depend on fibrinogen level, but also on combination effect of chemical and physical interactions in blood, including LDL-C level, glucose level, and smoking.²³ Fibrinogen was involved in subclinical phase of coronary and extracoronary atherosclerosis, had atherogenic effect in hyperlipidemia,³ and also related to the incidence of peripheral occlusive arterial diseases.²⁴ High fibrinogen level is risk factor for hypercoagulation that can obstruct the blood vessel, and when it occurred in heart blood vessel, there would be a risk of CHD development.⁴ However, it was still not clear, because high fibrinogen level did not obstruct blood vessel directly, except when there was hyperthrombosis in heart blood vessels. Plasma fibrinogen was an independent risk factor of CHD in men, but its role was not clear in women.^{25,26}

There were very few information on the association between plasma fibrinogen level and

coronary heart diseases in Asia. Plasma fibrinogen level in the Japanese was lower compared with the normal plasma fibrinogen level of people in Western countries. A study in Osaka showed that the mean plasma fibrinogen level was 267 mg/dL.²⁸ One mg/dL increase in fibrinogen level was associated with two times increased risk of death in 6 years. This result showed that fibrinogen did not only involve in pathogenesis of arterial disease, but also a strong independent predictor of mortality. There was a relationship between the increase in fibrinogen level and the severity of atherosclerosis, supported by data which suggested that local degradation of plasma fibrin of more than 350 mg/dL was a strong independent factor of brain and heart infarction.¹⁰ Infection might facilitate inflammation in atherosclerotic process. The increase in fibrinogen level in acute or chronic infection might increase the risk of cardiovascular disorders.²⁹ Patients with renal transplant suffered chronic prothrombotic reaction and persistent inflammation. The change in fibrinogen level and factor VIIc in patients with renal transplant was caused by the interaction between genetic and environmental factors, and this change supported the increased risk of cardiovascular diseases.³⁰ Obese patients also tended to have increased fibrinogen levels.³¹ This study found that controls had higher fibrinogen level than dyslipidemic patients and CHD patients, but this was not significantly different. Moreover, logistic regression analysis showed that fibrinogen was not a risk factor of CHD.

CONCLUSION

In this study, it was concluded that the change in lipid profiles was risk factor of CHD, but it was not the case for the change in plasma fibrinogen level.

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